## REMARKS

### Amendments to the Claims

Claims 25-26 and 33-75 are now pending.

Applicants herein re-introduce previously pending claims 18-24 and 27-32 as new claims 63-75 and also amend the dependency of claims 25 and 26 accordingly. Applicants also introduce minor amendments to claims 37-38 and 52-53. As claims 18-32 were previously pending and under examination, while the amendments to claims 37-38 and 52-53 are merely directed to matters of form, none of the instant claim amendments introduce new matter or require further search of the art. All of the claims are supported by the application as a whole. Applicants respectfully request the entry of the amendments.

The Office also holds claims 25 and 26 withdrawn as those claims had depended from a cancelled claim. That cancelled claim, number 18, is now reintroduced as claim 63. Hence, that withdrawal is now moot.

### Objections to the Claims

The Office first objects to claims 33, 36-48, and 51-62, asserting that those claims contain non-elected subject matter due to a prior election of species. According to the policy of M.P.E.P. § 803.02, Applicants expect that the Office will continue to examine that non-elected subject matter to the extent necessary to determine patentability once the Office finds the elected species to be allowable.

The Office also objects to claims 33-47, contending that the words "protease activating" in those claims are "easily misconstrued." Applicants do not amend those claims and request the withdrawal of the objection.

First, claims are construed in light of the application as a whole. *Phillips v. AWH Corp.*, 415 F.3d 1303 (Fed. Cir. 2005) (*en banc*). The specification uses the phrase "protease activating blood clotting factor VII" as a name for the claimed protease in numerous locations. (*See* the Title, first paragraph on page 1, final paragraph on page 6, second full paragraph on page 7, and first paragraph on page 9.) Moreover, the specification explains that the claimed protein is, in fact, the protease that activates factor VII *in vivo*. (*See, e.g.,* the second full paragraph on page 2.) Accordingly, one of ordinary skill in the art cannot fail to understand that the phrase is the name of the claimed protein. Second, Applicants wish to maintain consistency with the claim language the Office has already approved and issued in the parent patent and other related patents. *See, e.g.,* U.S. Patent No. 6,670,455 B1, at claim 1, reciting the same phrase. Accordingly, Applicants request that these objections be withdrawn.

**Claims 33 and 48 Are Definite Under 35 U.S.C. § 112, Second Paragraph**

The Office raises several new grounds of rejection in this Office Action. The Office now rejects claims 33 and 48 under 35 U.S.C. § 112, Second Paragraph, asserting that those claims, and therefore their dependent claims, are indefinite.

First, the Office contends that claims 33 and 48 lack antecedent basis for the phrase "the protease activating blood clotting factor VII." (Office Action at page 3.) Second, the Office contends that claim 48 is indefinite due to the phrase "a pure form of the protease activating blood clotting factor VII and a pure form of a proenzyme of said protease." The Office apparently wants to know how the proenzyme is activated to form the protease. (Office Action at page 4.)

Applicants traverse those rejections.

The standard for definiteness according to M.P.E.P. § 2173.02 is one of reasonableness, not absolute precision. That standard is based upon how one of ordinary skill in the art, who has read the specification in full and who is aware of the related art, would understand the claims. M.P.E.P. § 2173.02; *and see Phillips v. AWH*, 415 F.3d 1303 (Fed. Cir. 2005) (*en banc*) (explaining that claims are interpreted in light of the specification as a whole). The M.P.E.P. counsels examiners that claims that are otherwise clear to one of ordinary skill in the art within the context of the application as a whole should not be rejected merely because they might have been phrased differently. M.P.E.P. § 2173.02.

As explained above, one of ordinary skill would no doubt recognize that the phrase "the protease activating blood clotting factor VII" in claims 25, 33, and 48 is the name given to the specific protein being claimed. The fact that the phrase starts with the word "the" does not make it indefinite, especially as that phrase is used in the title and repeatedly throughout the application. (*See, e.g.,* the Title, first full paragraph at page 1, second paragraph at page 1, first full paragraph at page 3, and original claim 1.)

Similarly, the protease and its proenzyme are discussed throughout the text of the application as a whole, leaving one of ordinary skill in the art in no doubt as to the metes and bounds of the proteins that claim 48 covers. (*See, e.g.,* the Title, second paragraph at page 1, and the remaining text of the application as a whole, which discusses the protease and proenzyme on every page or nearly every page.) Hence, no amendment is needed as claim 48, like claim 33, is already definite.

Hence, Applicants request the withdrawal of those rejections.

As an aside, Applicants also note that the Office (via the present Examiner) has already issued at least two United States patents containing the same phrases that are now being rejected here. Those patents are Nos. 6,573,056 and 6,670,455, the latter of which is the parent of the instant application. Thus, Applicants urge the Office to maintain a consistent policy when examining the claim language in these cases.

**Claims 18-62 are Supported by the Application as a Whole, under 35 U.S.C. § 112, First Paragraph**

The second of the Office's new grounds of rejection is an assertion that the pending claims are not sufficiently supported by the application as a whole because the claims allegedly recite only partial sequences rather than complete sequences for those proteins. (Office Action at pages 4-6.) Applicants traverse that rejection.

Written description support is judged from the standpoint of one of ordinary skill in the art. M.P.E.P. § 2163. The standard for written description is whether one of ordinary skill in the art would reasonably conclude from the application as a whole and the prior art that the applicant had possession of the claimed invention. *See* M.P.E.P. § 2163(I).

Under that standard, "there is no *per se* rule that an adequate written description of an invention that involves a biological macromolecule must contain a recitation of known structure." *Falkner v. Inglis*, 448 F.3d 1357, 1366-1367 (Fed. Cir. 2006). The Federal Circuit made that clear, for example, when it overruled a decision of the Board of Patent Appeals and Interferences in *Capon v. Eshhar*, 418 F.3d 1349, 1360-61 (Fed. Cir. 2005), and again in the cases of *Invitrogen Corp. v. Clonetech Labs., Inc.*, 429 F.3d 1052, (Fed. Cir. 2005) and *Falkner v. Inglis*, 448 F.3d at 1367-68 (Fed. Cir. 2006).

Each of those cases dealt with claims to proteins or nucleic acid constructs that did not recite sequences. However, it was clear to the Court in each instance that the patent applicants possessed the claimed proteins or nucleic acids because skilled artisans could have found sufficient information to obtain the claimed molecules from the general guidance provided in the applications and from the scientific literature. For example, in *Falkner v. Inglis*, the Court specifically emphasized that the written description requirement "does not state that every invention must be described in the same way" such as via sequences. *Falkner*, 448 F.3d at 1368 (quoting *Capon v. Eshhar*, 418 F.3d at 1358). Instead, the level of support evolves as the knowledge pertaining to each field of research evolves. *Id.*

Here, Applicants provide partial sequences of the protein in the specification at page 1. In addition, Applicants also provide references to related German application 19 603 693.4 and the Choi-Miura article, at page 1 of the specification. Applicants also describe in detail a blood plasma purification scheme to specifically isolate the protease and proenzyme in pure form, as claimed. Moreover, those of ordinary skill in the art of blood factor proteins would know that each blood factor, such as Factor VII, is generally activated by a specific activating protease. From the name of the instant protease and its proenzyme, and the sequence information in the application text, one of ordinary skill in the art would understand that Applicants are referring to a specific protein in its protease and proenzyme forms.

Therefore, no more than what is disclosed in the instant application is needed to show that applicants were in possession of the instant compositions, and Applicants request the withdrawal of this rejection.

**Claims 18-62 are Enabled Under 35 U.S.C. § 112, First Paragraph**

Next, the Office now rejects the pending claims, asserting that they are not enabled throughout their full scope. (Office Action at pages 7-12.) The Office also bases that assertion on the fact that the claims do not include the full sequence of the claimed protease and proenzyme.

Applicants also traverse that rejection.

As Applicants have explained above, the instant application refers to German Application No. 19 903 693.4 for identification and further information regarding the discovery of the proenzyme and its protease. (*See* the Specification at page 1, second paragraph.) The application also devotes considerable discussion to methods of obtaining that particular proenzyme and its protease from blood plasma samples, which methods are also claimed in the parent patent 6,670,455 B1. (*See* the working examples.) In addition, to help one of ordinary skill to verify that he has purified the correct protein, the instant application also provides some partial sequences. (See the Specification at page 1, second paragraph.) The application also explains that the instant protease activates factor VII, serving as the basis for a simple activity test following purification of the protease. Thus, extensive information is provided in the application about how to purify the instantly claimed protease and proenzyme from blood plasma, and how to test its sequence and activity. There is no need for further information to enable the instant claims.

As to the Office's comments regarding a composition that comprises a mixture of the protease and proenzyme (see claims 48-62; Office Action at pages 8-12), the instant specification teaches methods for purifying each separate form of the protein.

(See Examples 1 and 2.) Such methods are also a subject of the issued parent patent, U.S. Patent No. 6,670,455. Certainly, such pure samples could then be mixed together to form compositions according to 48-62. Accordingly, the specification provides more than adequate guidance on preparing the formulations of claims 48-62.

Thus, Applicants request the withdrawal of these rejections.

**Claims 33-36, 38-39, 43-47, and 63-75 Are Nonobvious according to 35 U.S.C. § 103**

Finally, the Office rejects claims 33-36, 38-39, and 43-47 as allegedly obvious over Choi-Miura et al. (*J. Biochem.* 119: 1157-1165 (1996); "Choi-Miura") in combination with Turner et al. (U.S. Patent No. 5,326,558; "Turner"). (Office Action at pages 13-15.) The Office had previously also rejected claims 18-24 and 27-32 over the same combination of documents. (*See* Office Action of April 7, 2006). Those claims are now re-numbered 63-75.

Applicants also traverse those rejections.

An evaluation of obviousness involves:

(A) Determining the scope and contents of the prior art;

(B) Ascertaining the differences between the prior art and the claims in issue;

(C) Resolving the level of ordinary skill in the pertinent art; and

(D) Evaluating evidence of secondary considerations.

*See* M.P.E.P. § 2141; *Graham v. John Deere Co.*, 383 U.S. 1 (1966).

Here, claims 63, 33, and 48 require a pure form of the protease and/or the proenzyme of the protease. Choi-Miura and Turner, taken together, do not teach or suggest how to obtain either a pure protease of claim 63 or pure proenzyme of claim 33.

Accordingly, the also do not teach or suggest how to obtain a mixture of those pure forms as claimed in claim 48.

Indeed, Choi-Miura does not describe the purification of any particular form of the protein it calls PHBP. Examining Figure 1 of Choi-Miura, at page 1159, for example, it appears that Choi-Miura and co-authors obtained the PHBP protein from blood plasma in two or more bands. This indicates that what they obtained was a mixture of the two forms of the protein. In other words, while Choi-Miura and co-authors purified the protein in general in the sense of separating it from other components of blood plasma, they did not produce pure forms of the protease and proenzyme separately, as claimed in claims 63 and 33. Such a result is expected, given that the protein exists in both forms *in vivo* and given that proteases in blood plasma can contaminate isolation schemes, cleaving a proenzyme to its protease, and also further cleaving the protease to yet other smaller species.

Choi-Miura does not teac or suggest how to obtain a pure form of the protease or a pure form of the proenzyme. Indeed, Choi-Miura and co-authors would not have been interested in resolving those two different forms, as their object was merely to chop the protein to small pieces and to determine component amino acid sequences for those pieces. (See Choi-Miura at page 1159, Figure 2.) Such an analysis does not require pure forms of the proenzyme and protease.

It is only Applicants who have devised a preparatory scheme that specifically purifies the protease and specifically purifies the proenzyme. To purify the proenzyme, for example, Applicants identified conditions, such as a pH range that de-activates contaminating plasma proteases, thus preventing the proenzyme from being cut apart

during the purification process. Applicants discovered, for instance, that modifying conditions such as pH helped to avoid unwanted cleavage of the proenzyme. The process that Applicants developed is described, for instance, in the specification at page 3, last paragraph, to page 5, line 3. Example 2 further describes a purification of the proenzyme form of the claimed protein.

Choi-Miura also does not describe any compositions comprising the claimed pure protease or pure proenzyme, or mixtures thereof with the additional ingredients of claims 34-47, 49-62, and 64-75. Nor does Choi-Miura suggest that any such compositions could act as biological test reagents, as recited in claims 47, 62, and 75. Indeed, because Choi-Miura did not know what the function of the protein it discovered was, that article certainly could not suggest how the protein could be useful as a biological test reagent.

The Office cites Turner only for discussion of protease inhibitors, as the Office concludes pertain to claims 34-36, 38, and 43-44. (Office Action at page 14.) Turner does not pertain to the instant protease or proenzyme or suggest the other elements of claims 33, 37, 39-42, or 45-75.

Thus, comparing the teachings of the prior art to the instant claims, it is evident that the combination of Choi-Miura and Turner cannot render any of claims 33-36, 38-39, 43-47, and 63-75 obvious. Accordingly, Applicants request the withdrawal of that rejection.

**Conclusion**

In view of the foregoing amendments and remarks, Applicants request the withdrawal of all of the objections and rejections, and submit that this application is in

condition for allowance. Hence, Applicants respectfully request the allowance of all of the subject matter of claims 25-26 and 33-75 and the re-joiner of any non elected limitations within those claims.

This reply is submitted within one month of the receipt of the Office's Notice of May 2, 2007. Please grant any extensions of time required to enter this response and charge any required fees to our deposit account 06-0916.

Respectfully submitted,

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